REMARKS

Status of the Application

Claims 1-4, 6-11, and 15-27 were pending in the application at the time the Office Action was mailed. Claims 1-4, 6-11, 15-23, 25 and 26 were rejected. Claims 24 and 27 were objected to.

In this reply, claims 1, 2, 4, 9-11, 15, and 18 have been amended; claims 7, 8, 17, 24, and 27 have been canceled; and new claims 30 and 31 have been added. Therefore, claims 1-4, 6, 9-11, 15, 16, 18-23, 25, 26, 30, and 31, as amended, are pending. Consideration of these claims is respectfully requested.

Claim Objections

Claims 24 and 27 were objected to for being in improper multiple dependent form. Claims 24 and 27 have been canceled.

Rejections Under 35 U.S.C. 112

Claim 4 was rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the examiner:

> The specification teaches that the LucCDABE operon contains five genes necessary for self-sustained bioluminescence in bacteria: LuxAB is a luciferase, which catalyzes the light-producing reaction; LuxCE is a multi-component enzyme that converts myristic acid to a fatty aldehyde substrate for the light-producing reaction; and LuxD is a transferase that assists LuxCE (e.g., paragraph bridging pages 5-6). The specification

> teaches nucleic acid constructs comprising *luxA* and *luxB* genes in addition to *luxC*, *luxD*, and *luxE* genes (e.g., page 16, lines 22-27). Claim 4 reads on embodiments where the nucleic acid construct comprises *luxA*, *luxC*, *luxD*, and *luxE* genes, or a construct comprising *luxB*, *luxC*, *luxD*, and *luxE* genes. These combinations are not supported by the specification, claims or drawings as originally filed in that the specification teaches that both *luxA* and *luxB* are required in addition to the *luxC*, *luxD* and *luxE* genes for all proteins necessary for production of bioluminescence without addition of an exogenous substrate. The response does not point to portions of the specification, claims or drawings as originally filed as support for the amendment of claim 4. Therefore, claim 4 represents a departure from the specification, claims and drawings as originally filed.

To address this rejection, claim 4 has been amended to depend from claim 1, rather than claim 3. Thus, claim 4 no longer includes the limitation of a purified nucleic acid "wherein said gene cassette encodes all proteins necessary for production of bioluminescence without addition of an exogenous substrate."

Claims 1-4, 6-11, 15-23, and 25-26 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 7 and 8 have herewith been canceled. Although Applicants neither agree nor acquiesce in the rejections set forth in the Office Action, for the sole purpose of expediting prosecution of the application, claim 1 has been amended to recite "a modified protein selected from the group consisting of: a modified LuxA comprising an amino acid sequence in its carboxy terminus that specifically binds to a tail-specific protease, and a modified LuxB comprising a PEST sequence in its carboxy terminus that specifically binds to a protein associated with a ubiquitin-proteasome pathway, wherein the amino acid that specifically binds to a tail-specific protease results in a reduced half-life of the modified LuxA protein when

expressed in a bacterial cell compared to the half-life of the wild-type form of the LuxA protein when expressed in the bacterial cell, and wherein the PEST sequence results in a reduced half-life of the modified LuxB protein when expressed in a yeast cell compared to the half-life of the wild-type form of the LuxB protein when expressed in the yeast cell."

Applicants submit that amended claim 1 is fully enabled by the specification. The limitations of a "modified LuxA comprising an amino acid sequence in its carboxy terminus that specifically binds to a tail-specific protease...wherein the amino acid sequence that specifically binds to a tail-specific protease results in a reduced half-life of the modified LuxA protein when expressed in a bacterial cell compared to the half-life of the wild-type form of the LuxA protein when expressed in the bacterial cell" find support, for example, on line 2, page 9 spanning line 13, page 10; lines 1-17, page 11; Table 1, page 12; Table 2, page 13; lines 5-15, page 14; lines 10-23, page 15; and lines 3-8, page 16. Although numerous amino acid sequences that specifically bind tail-specific proteases were known prior to the filing date of the present application, the scope of amended claim 1 does not include every possible amino acid sequence that specifically binds a tail-specific protease in the universe of different amino acid sequences that specifically bind tail-specific proteases. Rather, the scope of amended claim 1 covers only those amino acid sequences that specifically bind tail-specific proteases that result in a reduced half-life of a modified LuxA protein having the amino acid sequence in its carboxy terminus when the modified LuxA protein is expressed in a bacterial cell compared to the half-life of the wild-type form of the LuxA protein when expressed in the bacterial cell.

Similarly, the limitations of a "modified LuxB comprising a PEST sequence in its carboxy terminus that specifically binds to a protein associated with a ubiquitin-proteasome pathway....wherein the PEST sequence results in a reduced half-life of the modified LuxB protein when expressed in a yeast cell compared to the half-life of the wild-type form of the LuxB protein when expressed in the yeast cell" find support in the specification. See, for example, lines 2-23, page 9; lines 14-28, page 10; lines 1-17, page 11; lines 10-11, page 15; and line 2, page 16 spanning line 5, page 17. Again, although numerous PEST sequences were known prior to the filing date of the present application, the scope of amended claim 1 does not include every possible PEST sequence in the universe of different PEST sequences and derivatives thereof. The scope of amended claim 1 covers only those PEST sequences that result in a reduced half-life of a modified LuxB protein containing the PEST sequence when expressed in a yeast cell compared to the half-life of the wild-type form of the LuxB protein when expressed in the yeast cell.

Thus, for the reasons cited above, the subject matter of claim 1 clearly meets the requirements of the enablement portion of 35 U.S.C. 112, first paragraph.

The Office Action states that the specification is enabling for a purified nucleic acid construct comprising a gene cassette encoding (1) a modified LuxA comprising a carboxy-terminal sequence selected from the group consisting of SEQ ID NOs: 8, 9 and 10, wherein the half-life of the modified LuxA protein when expressed in an *E. coli* cell is shorter than the half-life of the wild-type form of the protein when expressed in the *E. coli* cell and (2) a modified LuxB comprising the PEST-rich 178 amino acid carboxy-terminal sequence of G1 cyclin Cln2, wherein the half-life of the modified LuxB protein

when expressed in a yeast cell is shorter than the half-life of the wild-type form of the protein when expressed in the yeast cell.

Claims 9 and 18 have been amended to comport with what the Office Action states is enabled to expedite prosecution of this application. Claim 9 has been amended to recite "[a] purified nucleic acid construct comprising a gene cassette encoding a modified LuxA comprising a carboxy-terminal sequence selected from the group consisting of SEQ ID NOS: 8, 9, and 10, wherein the half-life of the modified LuxA protein when expressed in an *E. coli* cell is shorter than the half-life of the wild-type form of the LuxA protein when expressed in the *E. coli* cell." Claim 18 has been amended to recite "[a] purified nucleic acid construct comprising a modified LuxB comprising the PEST-rich 178 amino acid carboxy terminal sequence of G1 cyclin Cln2, wherein the half-life of the modified LuxB protein when expressed in a yeast cell is shorter than the half-life of the wild-type form of the LuxB protein when expressed in the yeast cell."

Because the enablement requirement of 35 USC 112, first paragraph, for each of the pending claims has been satisfied, withdrawal of these rejections and allowance of all pending claims is respectfully requested.

Conclusion

The currently pending claims before the examiner are supported throughout the specification and are patentable over the prior art. No new matter has been added. This application is now in full condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge the required fee for the additional claims and any underpayment or credit any overpayment of fees under 37 CFR 1.16 or 1.17 as required by this paper to Deposit Account 50-3110.

The examiner is cordially invited to call the undersigned if clarification is needed on any matter within this amendment, or if the examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

Date: May 10, 2006

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Docket No. 6704-29